REMARKS

Claim Amendments

Claims 1, 3, and 6 are amended to recite that Tome-1 activities are selected from the group consisting of: (1) modulating ubiquitinylation of wee1 protein; (2) modulating degradation of wee1 protein (3) modulating SCF complex components; (4) modulating entry of a cell into the cell cycle; (5) modulating progression of a cell through the cell cycle; (6) modulating release of a cell from the cell cycle; (7) modulating cell growth; (8) modulating cellular proliferation; (9) modulating tumorigenesis; and (10) modulating mitogenesis. Support for this amendment is found at page 17, lines 1-12.

Claims 1, 3, and 6 are amended to recite "modulating ubiquitinylation of wee1 protein." Support for this amendment is found in Figure 9 and page 10, lines 12-15:

> (A) shows Tome-1 addition enhances ubiquitinylation of wee1 in *Xenopus* egg extracts. Left: *in vitro* translated, ^{35}S-labeled wee1 was added to *Xenopus* egg extracts in the presence of absence of recombinant Tome-1 (+/- Tome-1), GST-ubiquitin (GST-UB), or methyl-ubiquitin (methylUb). (B) shows quantification of wee1 ubiquitinylation shown in Part A.

Claims 1, 3, and 6 are amended to recite "modulating degradation of wee1 protein." Support for this amendment is found, for example, in Figure 8 and page 9, lines 6-19-23:

> *Figures 8A-8F* depict Tome-1 is required for mitotic entry and wee1 degradation (A) shows degradation of the nuclear pool of wee1 requires Tome-1. Autoradiograph showing extent of ^{35}S-labelled wee1 degradation observed in a Tome-1-depleted (Tm1 Dep.) or mock-depleted (Mock Dep.) extract after isolating nuclei. (B) shows expression of ΔN-Tome-1 inhibits wee1 degradation in 293 cells.

Claims 1, 3, and 6 are also amended to recite that the SCF complex consists of SKP-1, Cul-1, Rbx, and an F-Box substrate receptor protein. Support for this amendment can be found at page 2, lines 20-21.

Claim 1, 3, 5, and 6 are also amended to recite that the nucleic acids are from eukaryotic cells. Each of the mouse, human and Xenopus sequences are eukaryotic organisms, therefore, the nucleic acid from each of those species was isolated from eukaryotic cells. Additional support for this amendment is found at page 1, lines 1-3: "Progression through the *eukaryotic* cell cycle requires the coordinated activity of proteolytic triggers and kinase cascades. (King et al. (1995) cell 81:279)." (emphasis added).

Claim 2 is cancelled.

Claims 1, 7-13 and 26 Are Definite Under 35 U.S.C. § 112, Second Paragraph

Claims 1, 2, 7-13 and 26 were rejected as indefinite for various reasons.

The Office Action states that it is not clear what activities "Tome-1 activities" encompasses. Claims reciting "Tome-1 activities" have been amended to recite which activities are encompassed by the phrase "Tome-1 activities." The meaning of Tome-1 activities is therefore clear. Please withdraw the rejection.

The Office Action states that it is not clear what Applicants intend as being encompassed by wee1 in claim 2. Claim 2 has been cancelled. Claims 1, 3, and 6, as amended, recite wee1 and those claims makes clear that Applicants refer to the wee1 protein. Therefore, Applicants request that this rejection be reconsidered and withdrawn.

The Office Action states that it is not clear what Applicants intend as being encompassed by an SCF complex component in claim 2. Claim 2 has been cancelled. Amended claims 1, 3,

and 6 recite SCF complex components and those claims clearly define the components as Skp-1, Cul-1, Rbx and an F Box substrate receptor protein. The meaning of SCF complex is therefore clear. Applicants request that this rejection be reconsidered and withdrawn.

The Office Action states that the meaning of what is encompassed by the recitation in claim 2 of SCF complex component activity is unclear. This rejection is moot as claim 2 is cancelled.

Applicants respectfully submit that the pending claims are definite. Therefore, Applicants request that all rejections under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

Claims 1, 3-13 and 26 Are Adequately Described under 35 U.S.C. § 112, First Paragraph

Claims 1, 3-13 and 26 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Office Action contends that the human, Xenopus, and mouse Tome-1 sequences are not "adequate written description of the genus claimed," Office Action at page 5, because the scope of the claims encompasses "unicellular and multi-cellular prokaryotes, which have vastly different sequences of DNA, protein and cell-cycles, i.e., lacking mitosis," *Id.*, and further because the claims "are not limited to those . . . Tome-1 activities listed on pg. 16 of the Remarks (in Applicants' prior response), and therefore all other non-biological and biological activities of Tome-1 are still encompassed by the claims." *Id.*

Applicants have amended claims 1, 3, and 5 to explicitly recite the following Tome-1 activities: (1) modulating ubiquitinylation of wee1 protein; (2) modulating degradation of wee1 protein (3) modulating SCF complex components; (4) modulating entry of a cell into the cell cycle; (5) modulating progression of a cell through the cell cycle; (6) modulating release of a cell from the cell cycle; (7) modulating cell growth; (8) modulating cellular proliferation; (9) modulating tumorigenesis; and (10) modulating mitogenesis.

Applicants note that one of skill in the art would understand that the unicellular and multi-cellular prokaryotes that do not undergo mitosis would not have a protein that would trigger mitotic entry. Nevertheless, to advance prosecution, Applicants have amended claims 1, 3, and 5 to recite that the nucleic acid sequence is from a eukaryotic cell.

The claims, as amended, are adequately described.

To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of compositions or methods, it must be clear that: (1) the identifying characteristics of the claimed compositions or methods have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

With respect to polypeptides, the U.S. Patent and Trademark Office's Written Description Guidelines state:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by . . . disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by ***functional characteristics*** coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. . . .

66 Fed. Reg. 1099, 1106 (January 5, 2001), internal reference omitted, approved in *Enzo Biochem., Inc. v. Gen-Probe Incorporated*, 296 F.3d 1316, 1325, 63 U.S.P.Q.2d (BNA) 1609, 1613 (Fed. Cir. 2002), emphasis added.

Description of a representative number of species does ***not*** require the description to be of such specificity that it would provide individual support for each species that the genus embraces (MPEP 2163 II (A)(3)(a)(ii)). *Id.* What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. *Id.*

Applicants respectfully submit that the instant specification more than adequately describes the claimed methods with reasonable clarity to one of skill in the art. Applicants teach a combination of identifying characteristics sufficient to show that Applicants were in possession of the claimed genus of ***eukaryotic*** nucleic acid sequences. Specifically, Applicants teach Tome-1 nucleotide sequences and the corresponding Tome-1 polypeptides, which have a specific sequence identity and the ***functional characteristic*** of having one or more ***recited*** Tome -1 activities.

One of skill in the art would recognize that Applicants had possession of the claimed sequences at the time of filing. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this rejection.

Claims 1-13 and 26 Are Enabled

Claims 1-13 and 26 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement.

The Patent Office contends that "it would be undue experimentation for one of skill in the art to test all of the representative DNA of all organisms, i.e., prokaryotes, eukaryotes, as well as archaic species." Office Action at page 5.

Applicants have amended claims 1, 3, and 5 to recite that the nucleic acid sequence is from a eukaryotic cell.

Applicants have also amended claims 1, 3, and 5 to explicitly recite the following Tome-1 activities: (1) modulating ubiquitinylation of wee1 protein; (2) modulating degradation of wee1 protein (3) modulating SCF complex components; (4) modulating entry of a cell into the cell cycle; (5) modulating progression of a cell through the cell cycle; (6) modulating release of a cell from the cell cycle; (7) modulating cell growth; (8) modulating cellular proliferation; (9) modulating tumorigenesis; and (10) modulating mitogenesis.

The claims, as amended, are enabled for their entire scope.

35 U.S.C. §112, first paragraph, requires that the specification must enable a person skilled in the art to make and use the claimed invention. The issue of adequate enablement depends on whether one skilled in the art could practice the claimed invention without undue experimentation. Enablement is not precluded by the necessity of some experimentation such as routine screening, even if it is ***extensive routine screening***. Also, the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (MPEP 2164.01) if the level of skill in the art is high or if all of the methods needed to practice the claimed invention are well known. *In re Wands*, 8 U.S.P.Q. 2d 1400, 1406 (Fed. Cir. 1988).

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. (Citations omitted). The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 8 U.S.P.Q. 2d at 1404.

Determining whether the nucleic acid sequence encodes a polypeptide having the claimed sequence identity and has one or more of the recited Tome-1 activities would involve only ***routine screening*** of ***eukaryotic*** sequences. This experimentation is not undue.

The pending claims recite amino acid or nucleic acid sequences having a specific amino acid sequence identity (i.e., comprising at least 60% or at least 85% sequence homology to a specific sequence identifier (e.g., SEQ ID NO:2, SEQ ID NO:5 or the like). The instant specification teaches the nucleic acid sequences and amino acid sequences of mouse, human and *Xenopus* Tome-1, methods of identifying Tome-1 polypeptides and cDNA, and methods of determining the recited Tome-1 activities. Accordingly, based on these teachings, one of skill in the art could easily make and use the claimed amino acid or nucleic acid sequences and the claimed polypeptides having one or more Tome-1 activities.

For at least these reasons, Applicants' specification, coupled with the level of skill in the art, enables a person of skill in the art to make and/or use the claimed invention. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of amended claims 1, 3-13 and 26 under 35 U.S.C. § 112, first paragraph.

Claims 1, 3-13 and 26 Are Novel Over Walker et al.

Claims 1, 3-13, and 26 stand rejected under 35 U.S.C. § 102(b) as anticipated by Walker *et al.*, WO 2002/018575 because "SEQ ID NO: 3 of Walker et al shares 97% homology with

Applicant's SEQ ID NO: 5," and further because "SEQ ID NO: 3 has greater than 97% sequence identity with Applicant's SEQ ID NO: 5, and for that reason, the encoded polypeptide will have at least 60% sequence homology to Applicant's SEQ ID NO:2." Office Action at page 7.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Walker *et al.* fail to anticipate claims 1, 3-13, and 26 because Walker *et al.* do not teach or suggest all elements of the claims.

First, claims 1, 3-13, and 26 all recite an isolated nucleic acid or depend from claims having this element. However Walker *et al.* do not teach that their SEQ ID NO: 3 nucleic acid was isolated. Indeed, Walker *et al.* note that SEQ ID NOS: 1, 2, and 4-10 were isolated but stress that an isolated SEQ ID NO:3 was not part of their invention: "The invention provides an isolated cDNA having a nucleic acid sequence selected from SEQ ID NOs 1, 2, and 4-10 and the complements thereof." Page 2, lines 21-22. See also page 8, line 39 to page 9, line 1: "The invention also provides a cDNA, its complement, and a probe comprising the cDNA selected from SEQ ID NOs: 1, 2, and 4-10." Thus, Walker *et al.* do not teach that their SEQ ID NO:3 was isolated. Accordingly, Walker *et al.* do not anticipate the claims because they do not teach the claim limitation that the nucleic acid is an *isolated* nucleic acid.

Second, claims 1, 3, and 6 are amended to recite that the polypeptides have the following Tome-1 activities: (1) modulating ubiquitinylation of wee1 protein; (2) modulating degradation of wee1 protein; (3) modulating Skp-Cullin-F-box protein complex (SCF complex) components, wherein said complex consists of Skp-1, Cul-1, Rbx and an F Box substrate; (4) modulating entry of a cell into the cell cycle; (5) modulating progression of a cell through the cell cycle; (6)

modulating release of a cell from the cell cycle; (7) modulating cell growth; (8) modulating cellular proliferation; (9) modulating tumorigenesis; and (10) modulating mitogenesis. Walker *et al.* fails to anticipate these claims because nothing in Walker *et al.* teaches that a peptide encoded by Walker *et al.*'s SEQ ID NO:3 has any of these Tome-1 activities.

Walker *et al.* neither teaches nor suggests the *isolated* nucleic acid of Applicants' SEQ ID NO: 5. Furthermore, Walker *et al.* does not teach or suggest that their SEQ ID NO: 3 encodes a polypeptide with an amino acid sequence having 60% or more homology to an amino acid sequence encoded by Applicant's SEQ ID NO: 2 that has any of the listed Tome-1 activities. Accordingly, Walker *et al.* fail to teach or suggest all of Applicants' claim limitations. The claims are thus novel over Walker *et al.* Applicant respectfully requests withdrawal of the rejection.

CONCLUSION

Having addressed all outstanding issues, Applicants respectfully request reconsideration and allowance of the case.

Respectfully submitted,

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By

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